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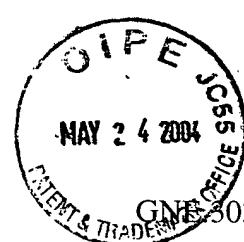
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GENENTECH INC.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Desnoyers, et al.
Appl. No. : 09/931,836
Filed : August 16, 2001
For : NOVEL PEPTIDES THAT
INDUCE CHONDROCYTE
REDIFFERENTIATION
Examiner : Jiang, Dong
Group Art Unit : 1646

DECLARATION OF LUC DESNOYERS AND WILLIAM I. WOOD
UNDER 37 CFR §1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

We, Luc Desnoyers and William I. Wood, declare and state as follows:

1. We are the inventors of the subject matter that is presently claimed in the above-captioned patent application.
2. During the time period in which all of the events and activities described herein occurred, we were employed by Genentech, Inc., the assignee of the above-captioned application.
3. All of the events and activities described herein were performed by us personally, or under our direction, as part of our duties as employees of Genentech, Inc.
4. The invention claimed in the above-captioned patent application was conceived prior to April 20, 1999 and diligently reduced to practice thereafter in the U.S. as described below.
5. Prior to April 20, 1999, we conceived of the polypeptides claimed in the above-captioned patent application. This is demonstrated by the attached sequence printout (Exhibit A), which was generated prior to April 20, 1999, and which shows the complete sequence of the polypeptide having the sequence of SEQ ID NO:2. The attached printout also shows the complete sequence of the nucleic acid which has the sequence of SEQ ID NO:1. As evidenced by the sequence printout, we were in possession of the complete polypeptide sequence prior to April 20, 1999.
6. The date deleted from page 1 of Exhibit A is a date prior to April 20, 1999, and was redacted pursuant to M.P.E.P. § 715.07. The redacted date is the date when the data were generated; the date the report was printed, April 16, 2004, remains on the report.

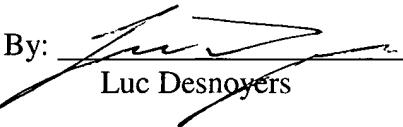
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7. After initially conceiving the polypeptide having the sequence of SEQ ID NO:2 prior to April 20, 1999, we diligently reduced the claimed subject matter to practice by working to express and purify the polypeptide and to run it systematically through many assays. The cDNA was deposited with the American Type Culture Collection (ATCC) on January 12, 1999 and assigned ATCC no. 203581. The protein of interest was assigned a "protein inventory number" (e.g., PIN1308 and PIN1308-1). As set forth in the enclosed Exhibit B, the polypeptide was expressed in *E. coli* - PUR1009 (see page 2) on November 16, 1998; in *Baculovirus* - PUR1039 (see page 3) on November 23, 1998; and in mammalian cells (see page 4) on February 17, 1999. Furthermore, various constructs with poly-His or IgG tags were made from the time of first cloning and the construction of these was followed by expression and purification of the protein during the time period of prior to April 20, 1999 through March 13, 2003. For example, Exhibit C shows July 13, 1999 as the date of purification of a polypeptide having the sequence of SEQ ID NO:2. PIN1308 and/or PIN1308-1 were distributed to various scientists for multiple cell-based assays and/or quality confirmation tests from August 20, 1999 through January 22, 2001.

8. Exhibits D and E list the assays performed on the purified protein. Assay ASY110, called "Chondrocyte Re-differentiation Assay" was completed on November 10, 1999 for PIN1308-1, which is a polypeptide having the sequence of SEQ ID NO:2. PIN1308-1 was delivered to Luc Desnoyers for one of the assay runs on October 22, 1999; testing was completed on November 10, 1999. Exhibit E is an assay result list that shows positive results for the assay completed on November 10, 1999, thereby confirming the ability of the claimed polypeptide to induce chondrocyte redifferentiation. Thus, actual reduction to practice occurred at least by November 10, 1999.

9. After reducing the invention to practice, we worked with the Genentech, Inc. patent department to prepare a non-provisional patent application, which included the sequence of SEQ ID NO:2, as well as the data showing the ability to induce chondrocyte redifferentiation. That application was filed on March 1, 2000.

10. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

By: 
Luc Desnoyers

Date: 5/17/04

By: 
William I. Wood

Date: 5/17/04

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EXHIBIT A

(16 pages; pages 4-19)

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EXHIBIT A—PAGE 1

```
>Friday, April 16, 2004  
>DNA44686 [Full]  
>584 Sites [All_Sites]  
>  
>Sequence confirmed by pitro.  
[DNA44686: shieldens]
```

insert starts here^

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EXHIBIT A—PAGE 2

ssrI
sacI
hgAI/asPHI [M. aluI-]
ecI136I-
bsP1286 [M. aluI-]
bsiBKA1
bmy-
banII [M. aluI-]
scrFI [dcm-]
pspGI
mvaI aluI
ecoriI [dcm-]
dsavI [dcm-]
bstXI
bsSI [dcm-]
mwcI bprI/gsuI [dcm-]
bstXI apI [dcm-]
101 AGACCACT CCTGGAGCTC TCTGAGAC AGACTCCAG AGACAGAAG AGTCCCTGT AGACTCCAG AGACACTTA GTACGAACC TCCGTCGAGT AGATACCGT TGAGGACCGA
1
N L W R Q L I Y W Q E L A
"NET
pleI
mlyI
hinfI bsrI
bstXI
14 L F L P F C L C Q D E Y N E S P Q T G G L P P D C S K C R G D Y
mnlI
mlyI
mspI
hpaII
bsaWI
sfcI
pstI
bsmAI
nialII sfc
20: TCTTTCCTCC TCCCTTTC CCTGTGICAA GGTGAAATACA TGAGTCCTCC AGAAACCGGA GAGTACCCC CAGACTGAG "TAAGTGTGT CATGGAGACT
AAGAAAGG AGGAAAGC GGACACAGT CTACTATG ACTCAGAGG TGTGTCCTCC CTGTGAGCTC ATTCACACAA GTACCTCTGA
-5-

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EXHIBIT A—PAGE 3

mwol
bgII [M.haeIII-]
sau36I [M.haeIII-]
sau96I [M.haeIII-]
pspOMI / bspI20I
nlaV scrFI [dcm-]
sau96I [dcm-] [M.haeIII-]
scrFI [dcm-] scrFI [dcm-]
pspGI scrFI [M.hpaII-]
mvaI nciI pspGI mvaI nlaIII
ecoriI [dcm-] haeIII/paII ecoRII {dcm-}
dsaV [dcm-] bspI286 [M.haeIII-] xcmI
ostNI mspl mvaI dsaV [dcm-]
bsaXI [dcm-] bmyI ecoRII [dcm-] styI
bsaII hpaII dsaV [dcm-] ncoI
sau96I [M.haeIII-] banII [M.haeIII-] bstNI dsal nlaII
xcmI nlaIV apy-[dcm+] apal bstNI bssKI [dcm-] nlaII
styI haeIII/paII dsaV bssKI [dcm-] htgi/bstDSI rcaI
mwol mnlI bsaJI bsaJII haeIII/paII apyI [dcm+] tsgrI hpy188I
aiul tagI mwol ecc0109I/draII bssKI mnlI bsmI apyI [dcm+] nlaIV bsrI bspHI
301 ACAGCTTCG AGCCACCAA GGCACCCCTG GGCACCGGG CCCTCCCTGGC ATTCAGGAA ACCATGGAA CATGGCAAC AATGGCAAC ATGGCTCA
TCAGGAAAGC TCCCTAIGGTT CGGGGGGAC CGGGGGCC CGGGGGCC CGGGGGCC TAACTCTT TGGTACCTT GTTACCTT GACCTGGT GACCTGAC
48 S F R G Y Q G P P G P P G I P F G I P G N H G N N G A T G H E

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EXHIBIT A—PAGE 4

taqI scrFI[M.hpaII-]
xbaI ncII
tliI msPI
scfI[dcm-] hpaII-
pPfGI smI dsAV
mvaI haeIII/palI bsaKI
ecoriI[dcm-] bsaJI
dsvI[dcm-] xmaI/pspA1
batNI paeR7I smI
bssKI[dcm-] scrFI[M.hpaII-]
bsaJI mciI mnOI
tsp45I sau96I[M.haeIII-] sau96I[M.haeIII-]
maeIII nlaIV avaiI[M.taqI-] nlaIV
hphI apyI[dcm+] mliI bsrBI tseI haeIII/palI
bsrBI fnu4HI/bsoFI bsaJI hinfI
bsrBI ec0010I/dr4II acII bbsI nlaII avaiI[M.hpaII-]
nlaIV hphI
40: AGGACCCAAA GCTGAGRAAGG GGCACACAGG TGACCTGGGG CCTCGAGGGG AGCGGGGCCA GCGTGGGCCA AAGGAGAGA AGGGCTACCC GGGGATTCCA
TCCCTGGGTCT CCACCTTTCC CGCTGTTCG ACTGGACCCC GGAGGCTCCC TTGCCCCCGT GTACCCGGGG TTTCCTCTCT TCCCGATGGG CCCCTAAGGT
81 G A Z G E K G D K G D L G P R G E R G Q H G P K G E K G Y P G I P
mnOI
hpy188I bsmI nlaIII tspRI
hpyChIV mnOI tsp45I hpy188I tspRI
ec057I hpyChIV mnOI hpy188I tspRI
501 CCAGAACTC AGATTCGCACT CATGGCTCT CTGGCAACCC ACTTCAGCAA TCGAAAGCT GGGTATTATCT TCAGGACTGT TGAGCCAC ATTGGAACT
GGCTTGAG TCTAACGTTAATGACGAGA GACCGTGGG TGAAGTCGTT AGTCCTGCTCA CCTTAATAGA ACTCGTCACA ACTCTGGTG TACCTTGA
114 P E L Q I A F M A S L A T H F S N Q N S G I I F S S V E T N I G N F

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EXHIBIT A—PAGE 5

sau96I [M.haeIII-]
 nlaIV
 haeII/pall
 sau96I [W.haeIII-]
 pspOM1/bsp126I
 n-aiIV
 eco0109I/draII
 bspI286 [M.haeIII-]
 bnyI
 banII [M.haeIII-]
 apaI
 bsrI
 rcaI
 hpy188I
 bspII
 bsrI
 601 TCTTGATGT CAGACTGGT AGAATGGGG CCCGAGTC AGGTGGTAT TCTCTACCT TCACTGAT GATGTTGAGG AAGTGATGT
 AGAACTACA GACTACCA TCAAACCC GGCGCATAG TCAACACATA AACGACTGGA AGTGCTACTA CTCGGTACTC CTACLACTCC TTGACATACA
 148 F D V N T G R F G A P V S G V Y F F T F S M K K H E D V E E V Y V

nlaIII
 nlaIV
 haeII/pall
 sau96I [W.haeIII-]
 pspOM1/bsp126I
 n-aiIV
 eco0109I/draII
 bspI286 [M.haeIII-]
 bnyI
 banII [M.haeIII-]
 apaI
 bsrI
 rcaI
 hpy188I
 bspII
 bsrI
 601 TCTTGATGT CAGACTGGT AGAATGGGG CCCGAGTC AGGTGGTAT TCTCTACCT TCACTGAT GATGTTGAGG AAGTGATGT
 AGAACTACA GACTACCA TCAAACCC GGCGCATAG TCAACACATA AACGACTGGA AGTGCTACTA CTCGGTACTC CTACLACTCC TTGACATACA
 148 F D V N T G R F G A P V S G V Y F F T F S M K K H E D V E E V Y V

rsalI
 csp6I
 bspI407I/bsrGI
 eco57I nlaIII
 mboII nspVI
 bpuAI nspI
 bbsI nwoI
 rsalI csp6I hpyCH4V
 70: GTACCTATG CACATCGCA ACCAGCTTC CAGATGTC AGCATGAAA TGATGGCA AICAGATACA TCCGGCATTC ATGGCTGTCT
 CATGGAAAC GTGATACCGT TGTCTAGAA GTCTAATG TGCTACTTT ATCTTCCGTT TACTCTATGT AGGCTGGTAG TACGACACCA CTTCTGARCC
 148 Y Z M Z N G N T V Z S M Y S Y E M R G K S D T S S N K H A V L K I A

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EXHIBIT A—PAGE 6

nlalII
styI
ncoI sau36I
dsal nlalIV
fokI tseI hinP1 btgI/bstDSI tfII
bstFSI bbvI bsrDI haeII hinfI
801 AAGGGGATG AGGTTCGGC GCGATGGCC AATGGGGCTC TCAATGGGA CACCAACGC TTCRCACCT TGCAGGAT CCTGCCTTT GAACTTAAGT
ITCCCCCTAC TCCAAACGA CGCTTACCGG TACCGCGAG AGTACCCCT GTGTTGCG AGAGGTGAA ANC GTCTAA GGACGAGAA CTTTGATCA
214 K D E V W L R M G N G A L H G D H Q R F S T F A G F L L F E T K O

mnII
ddel
bspCNI
ddel [M aluI-]
bspCNI
mboII celII/espI dpmI {dan-}
bsuAI bpfI/bpmI:021 dgnI {dan-} tro9I
b-fai aluI bslI bbsI aluI aluI maeIII hpy188I mseI mnII
90: AATGATAGC CTAGAAAGC TCACT-TGG GGAAGACTTG TAGCTGAGCT GATTGTTAC GATCTGAGGA AGCTAAAGT TGAGGGTTT ACATTCGCT
TITATTAATG GATCTATCG AGGTGAAACC CCTTCGAC ATGACTCGA CTAACATCG CTAGACTCT GTAAATTC AACTCCAAA TGTAGGACA

ddel
bsp1266 tfII dd
bmyI hpy188I mboII
banII bpfI bspCNI hinfI
bsrDI bsp509- hpyCHAY tfII
tsp509- sfaI csp6I tsp509I
1001 ATGCAAAATTTATGGT CAGTGTGCTACAG GTACACCAAT ATGTTGGAC ATICAGGGG CTCAGAGAA TCAACACAA ATAGCTCTC
TAACTTCCT ATTAACCAAC GTTACACAA GGCGATGTC CAGTGTGTA TCAACCTG TIAAGTCCC GAGTCCTCT AGTGGTGT TATCAGAG

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EXHIBIT A—PAGE 7

hpy188I nlaIV
 ddefI baiI mnII bspMI
 hpyC4V bspCNI styl bseRI hgaI
 hpyC4V bsaII tsp509I hpy188I ssPI
 1101 TCACTGACCT TTGACTAATA TCTTCGCGAT CTTCATCACT CTTCTTGG CACTAAGG ATTAATTCCTC TCTGAGCG AGTTCGCTCA
 ACTCTACGGS AACCTGATAC AGCAGCTGA AACAGCTGA GAAAGTGA GMAAGGAAACCTGAGG AGACTGCGTC TAACTAGGG CAACCTTAT AACAAAGAC
 tru9I
 tsp509I nlaIV
 tru9I bsrI hpy188II ecc57I maeI
 apoI mseI maeI
 hpyC4V tsp509I
 11261 TCACAGAGC CATTGCGAA GATTGCGAC TACTCTGCTT TTAATTAT ACCAGCTTC AGGAAACCCCT GAACTTAA GTCATATT CTTTATCCTA
 AGGTGCTCA GAAACGTT CTTAAACTG ATGAGCGAA AACAAATAA TGGTCAAAAG TCCCTGGGA CTTCAAAAT CTAAGTATAA GAATATTGT
 tsel
 Fnu4HI/HsoFI
 rnaI
 maeI
 mnII bbVI
 bstAPI bsp1286 bsp1286
 bsp1286 aluI bmyI
 bmyI bfaI mnII aluI
 hpy188I mnII
 tfII fokI bsp1286 aluI
 hinfl bstF5I
 1301 TTGAGGAA TCCGGTCAAG TGAATGACA GGGCTGGGC AGGACAGG GCACATAGCTG CCATATAGC TAATTAGTC CCTCCCTGT TCTGATCGAC
 AACCTCTCA AGCCATACATCAACTCTT CCGAACCCCG TTCTGTCCT CGGATATCGC ATTAAATTCG AACCTTACG AGCTGCTAC AGCTGCTAC

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EXHIBIT A—PAGE 8

sau3AI	mboI/ndel-[dam-] dpnI-[dar-] dprI-[dam-] alwI/dan-]	trp509I [K, ecoRI-] ecori trp509I mseI	tru9I mseI ahaiII/craI alwI	tru9I mseI bs
1401	CITGCCCTTTCCTT-TGAA GAACTGGAAAGGAAACI	TCATTAACCTCTGAACTTA ACGTCTTAACTGTTAGT ACGTCTTAACTGTTAGT ACGTCTTAACTGTTAGT	TATTTAAGTCATAGTAT TACATGTTACATGTTAC ATATATCTTACATGTTAC ATATATCTTACATGTTAC	TTACATGTTACATGTTAC ATATATCTTACATGTTAC ATATATCTTACATGTTAC ATATATCTTACATGTTAC
1450	tsp509I	bsII hpy88I bsII hpy88I	bsII hpy188I bsII hpy188I	bsII hpy188I bsII hpy188I
1501	CAGTAATGIGGTTGAAATT GTCATACAC	TGTTGATGTT CCCCACCATC GCCCCAACT TCGGATGTT GCTCAGGAGG TCAAGGTCA CTATTAAC GAACTAACAA ACACATCAA GGGGGTGAG AGCCATACCC CCAGTCCTCC	TGTTGATGTT CCCCACCATC GCCCCAACT TCGGATGTT GCTCAGGAGG TCAAGGTCA CTATTAAC GAACTAACAA ACACATCAA GGGGGTGAG AGCCATACCC CCAGTCCTCC	TGTTGATGTT CCCCACCATC GCCCCAACT TCGGATGTT GCTCAGGAGG TCAAGGTCA CTATTAAC GAACTAACAA ACACATCAA GGGGGTGAG AGCCATACCC CCAGTCCTCC
1550	tsp509I	bsII hpy88I bsII hpy88I	bsII hpy188I bsII hpy188I	bsII hpy188I bsII hpy188I
1601	rsAI csp62- mnlI bsI4CI/hp4CH4II	mlaIII nspHI nspI hpyCH4V	mlaIII nspI hpy188I hpy188I	mlaIII nspHI nspI hpy188I
				mbcII eco57I aseI/asnl/vspI aseI/asnl/vspI bs
				tru9I mseI aseI/asnl/vspI aseI/asnl/vspI bs

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EXHIBIT A—PAGE 9

190 ATAGING
CAT-TAC

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EXHIBIT A—PAGE 10

> length: 1966		GSeqEdit, DNA46686 (Philly), page 10			
acc1 (GTMKAC) :	1032				
aci1 (CCGC) :	452	1815	1819	1870	
af1II1 (ACRYGT) :	77				
ahalII1 (TTTAAA) :	1464				
alui1 (AGCT) :		116	275	303	741
alw1 (GGATCKNNN) :		793	918	942	947
apai1 (GGGCC) :		1356	1368	1393	1483
apoI (RATTY) :		116	275	303	741
apy1 (CCGGI) :		793	918	942	947
ase1 (ATTAAT) :		116	275	303	741
asn1 (ATTAAT) :		793	918	942	947
aspI1 (GMCNC) :		116	275	303	741
aval1 (CYCGRE) :		793	918	942	947
avalII1 (GGGCC) :		116	275	303	741
bamHII (GGATCC) :		793	918	942	947
baai1 (GGYRCC) :		116	275	303	741
banII1 (GRGCYC) :		793	918	942	947
bbbsI (GAAGACNNNN) :		116	275	303	741
bbbbr- (GCAGCC) :		793	918	942	947
bbef1 (CTAG) :		116	275	303	741
bbg1I (GCCNNNNNGGC) :		793	918	942	947
bbj1p1 (CTTNAGC) :		116	275	303	741
bbry1 (GGGCHC) :		793	918	942	947
bpn1 (CTCGAG) :		116	275	303	741
cpn11221 (GCTNAGC) :		793	918	942	947
cpn11 (GAAGACNNNN) :		116	275	303	741

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EXHIBIT A—PAGE 11

bsaI (GGTCCTCNRNNNN) :	100 582
bsaJ (CCNNGG) :	9 95 317 326 327 362 434 468 489 842 145 1873
bsaNT (NCCCGN) :	255
bscRI (CAGGAGNNNNNNNN) :	97 1167
bsgI (GTGCA G) :	4
bst:1236I (GGG) :	78 1820
bsiCI (TTCGAA) :	24
bsiEI (CGRYCG) :	1816
bsi:IKAI (GAGGCNC) :	115
bsII (CCNNNNNNNNGG) :	249 633 922 1544 1837
bsiAI (GTCCTC) :	10C 136 245 295 582
bsmAI (GTCCTC) :	100 136 245 295 582
bsmT I (GGGACNNNNNNNNNNNN) :	847
bsm: (GAATGCN) :	343 516
bsseFI (GCNGC) :	173 456 818 1357 1815 1818 1869 1894
bsp126 (ATCGAT) :	19
bsp120I (GGGCC) :	338 628
bsp1286 (GDDGHC) :	115 338 628 1068 1349 1378
bsp1407I (TGTACA) :	736
bspCN- (CTCAGNNNNNNNN) :	130 142 944 964 1071 1100 1123
bspDII (ATCGAT) :	19
bspHII (TCATA) :	395 610
bspM- (ACCTGC) :	1177 1836
bsrBI (GAGGG) :	450
bsrDI (GCAATGNN) :	829 992 1020
bsrGI (TGTACA) :	736
bsrI (AC-EGN) :	39 390 615 633 1252 1500
bsrK- (CCNGG) :	83 111 327 336 355 354 434 488 489 1713
bst4CI (ACGT) :	556 723 1615 1729
bstAPI (GCNNNNNTGCG) :	1351

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EXHIBIT A—PAGE 12

bsrB1 (TTGCAA) : 24
bsrBS1 (CCRYGG) : 362 842 1873
bsrE11 (GGTRACC) : 429
bsrF5I (GGATG) : 680 769 806 1313 1553
bsrEM1 (CCMGG) : 111 327 345 354 434 1713
bsrE11 (GGCG) : 78 1B20
bsrX1 (CCANNNNNTGG) : 104 1500
bsrY1 (RGATCY) : 46 57
bsrJ1 (CCRYGG) : 362 842 1873
bsrI1 (GGAGTGN) : 574
bsrB1 (GCNAGC) : 194 794
celI1 (GCTNAGC) : 943 1394
cfoI (GCCG) : 835
cfrI (GGGCC) : 32 41 1816 1867
claiI (ATCGAT) : 19
esp6I (GTAC) : 701 737 1041 1613
ddrE (CTRAG) : 130 142 895 944 964 1071 1160 1123 1395 1695
dpnI (GATC) : 47 58 961 1419
dpnII (GATC) : 47 58 961 1419
dralI (T^{TA}AA) : 1464
dralI (RGMCY) : 320 338 437 627 628
drclI (GACNNNNNGTC) : 72 1823
dsalI (CCRYGG) : 362 842 1873
dsavI (CCAGG) : 83 111 327 336 345 354 434 488 489 1713
esaI (YGCCR) : 32 41 1816 1867
eagI (GGCCG) : 1816
ec1136II (GAGCPC) : 115
ec1-X- (CGECCG) : 1616
eco57I (CTGAAG) : 507 542 569 659 728 789 1269 1667
econt (CCTNNNNAGG) : 1837

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EXHIBIT C—PAGE 13

ec001091 (RGGGNCY) : 320 338 437 627 628
ec0R1 (GAATTC) : 27 1044
ec0R1 (CCMGG) : 111 327 345 354 434 1713
esp. (GCINAGC) : 943 1394
fri49H1 (GCNGC) : 173 458 818 1357 1815 1818 1869 1894
fri211 (GGCG) : 78 1820
f041 (GGATG) : 680 769 806 1313 1553
gsl1 (CTGCA) : 112
haeII (RGCGCY) : 834
haeII (GGC) : 33 42 321 331 339 439 465 629 1817 1868 1877
hpaI (GACGC) : 79 1174
hpaI (GNGCAG) : 115
hhaI (GGC) : 835
h-np1 (GCGC) : 835
hincII (GTRAC) : 1645 1832
hindII (GTRAC) : 1645 1832
hirdII (AGCTT) : 1862
hinfI (GANTC) : 22 138 157 243 494 877 1078 1308 1823 1830
hpaII (CCGG) : 44 83 256 336 489
hpaII (GCTGA) : 411 429 655
hpy188II (TCNGA) : 141 509 551 762 963 1072 1101 1171 1311 1441 1551 1666
hpy188III (TCNGA) : 52 227 395 610 1259 1563 1826
hpyCH4II (ACNET) : 556 723 1615 1729
hpyCH2V (TCGA) : 5 276 515 709 872 1019 1215 1640 1839 1893
maeI (CTAG) : 53 795 911 1354 1827
maeII (GTWAC) : 430 956
mboI (GATC) : 47 58 961 1419
mboII (GAGA) : 126 568 652 727 932 1075 1096 1669
nciI (GTYCC) : 18 6
nruI (ACGCT) : 77

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EXHIBIT C—PAGE 14

mlu⁺ (GAGTCNNNN) : 138 243 1823 1830
xbaI (CCTC) : 9 50 62 68 97 144 173 209 259 310 342 441 445 670 687 810 966 982
.169 1362 1567 1573 1610 1653
msel (TAA) : 974 1241 1246 1277 1434 1465 1584 1684 1781
nsiI (CAYNNNNRTG) : 675
mspI (CCGG) : 44 83 256 336 489
mvaI (CCGG) : 111 327 345 354 434 1713
mviI (GCNNNNNNCC) : 78 1820
mwoI (CCGNNNNNN) : 34 198 164 304 313 340 452 516 525 733 1351 1360 1869
nciI (CCSGG) : 83 336 488 489
ncoI (CCATGG) : 362 842 1873
nfiI (GATC) : 47 58 961 1419
nhe⁺ (GCTAGC) : 794
nlaIII (CA₂C) : 161 239 291 363 396 462 521 611 665 675 734 780 843 1642 1674
nlaIV (GGNNCC) : 46 321 338 384 402 437 465 627 628 629 647 1149 1262
nre⁺ (GGGCCG) : 18.5
nspH⁺ (RCATG) : 733 1641
nspI (RCATG) : 733 1641
nseRT (CTCGAG) : 442
paiI (GGCC) : 33 42 321 331 339 439 465 629 1817 1868 1877
pblI (GAGTCNNN) : 138 243 1823 1830
pslI (TTATA) : 1233 1899
pspAI (CCCGGG) : 468
pspGI (CCGGG) : 111 327 345 354 434 1713
pspOKI (GGCCCC) : 338 628
psp-I (CTGGAG) : 275 1838
rcal (TCATGA) : 395 610
rmlI (CTAG) : 53 795 911 1354 1627
rsal (GTAC) : 70 737 1041 1613
sacI (GAGTC) : 115

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Filed : August 16, 2001

EXHIBIT C—PAGE 15

salI (GTCGAC) : 1832
sau3AI (GATC) : 47 58 961 1419
sau36I (GCNC) : 321 330 338 333 438 465 626 629 848 1877
scfI (TAGEGATAACAGGGTAA) : 1844
scfFI (CCNGC) : 83 111 327 336 345 354 434 488 489 1713
sfaNI (GCATC) : 87 1127
sfCI (CTYAG) : 275 299 1035 1838
sfII (GCCNNNNGCC) : 33 1868
sfUI (TTCGA) : 24
smal (CCCGGG) : 488
smbl (CTYAG) : 442
sppI (AATAT) : 1187
sstI (GRGCTC) : 115
styI (CCNGC) : 317 362 842 1146 1873
taqI (TCGA) : 20 25 64 70 308 443 1833
telI (GANTC) : 22 157 494 877 1078 1308
thaI (CGCG) : 78 1820
tliI (CTCGAG) : 442
tru9I (TTAA) : 974 1241 1246 1277 1434 1465 1564 1684 1781
tsseI (GCNGC) : 173 458 818 1357 1694
tsp45I (GTGAC) : 43C
tsp50I (AATP) : 28 1009 1061 1163 1222 1243 1372 1445 1516
tspRI (NNCACTGNN) : 38 389 557 575 1616
vspI (ATTAAT) : 1683
abaI (CTCAGA) : 52 1826
xcmI (CCANNNNNNNNNGG) : 311 362
xhoI (CTCGAG) : 442
xhoII (RGATCY) : 46 57
xmaI (CCCGGG) : 488
xmaIII (CGGCCC) : 1816

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EXHIBIT B

(4 pages; page 21-24)

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EXHIBIT B—PAGE 1

PRODUCTION HISTORY									
Order	UNQ	753	Search	UNQ	753	Search	UNQ	753	Search
Order	Protein	System	Request Name	PRO	Protein Request	EXP	PUR	Request	Protein
1. Order	DNA84665	E Coli	Human CTRP3 Poly-His	PRO1825		EXP2247	PUR1009	Done	
2. Order	DNA84665	E Coli	Human CTRP3 Poly-His	PRO1825		EXP2247	PUR4414	Done	
3. Order	DNA87982	Baculovirus	Human CTRP3 IgG	PRO1855		EXP2255	PUR1039	Drop	1
4. Order	DNA102368	Mammalian Stable	Human CTRP3 Poly-His	PRO4365		EXP2294			

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Filed : August 16, 2001

EXHIBIT B—PAGE 2

GENENGENES

[SITEMAP](#) [Additional Help](#)

[GENE VIEWER](#) [GENE](#) [FAM](#) [MAP](#) [GENEHUB](#)

[SEQUENCE VIEWER](#) [DNA](#) [SRC](#) [RNA](#) [LIB](#) [RS](#) [DOM](#)

[ASSAY VIEWER](#) [ASY](#) [FLS](#) [EXP](#) [PUR](#) [LOT](#) [ASV](#)

EXP2247

Gene Name: UNQ753 PRO 1825 Human CTRP3 Poly-His TFDNA84665 FLDNA44686

EXP Lab Name: pE44686-1

DNA Lab Name:

Protein Request ID:

System: E Coli

Expect Harvest Date:

Control: Control

Fermentation Run ID:

Cell Line:

Expression Media:

Growth Factors:

Supplements:

Wardrobe:

Gels:

Expressed: FALSE

Comments:

Status:

Date Entered: November 9, 1998

Date Canceled:

Scientist: Dan Yansura

Notebook: 0

Protein Lots: LOT2552 PIN1308-1

ASV | DNA | DOM | EXP | FAM | FLS | LIB | LOT | MAP | QLI | PRB | PRO | PUR | RNA | SRC | UNQ | XPT | YST
Assay Viewer | Sequence Viewer | Gene Viewer | GenenGenes | SAGE

GenenGenes Feedback

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 Filed : August 16, 2001

EXHIBIT B—PAGE 3

GENENGENES		SITEMAP		Additional F																	
GENEVIEWER	SEQUENCEVIEWER	ASSAYVIEWER	GENE	FAM	MAP	GENEINFO	GENE	FAM	MAP	GENEINFO	GENE	FAM	MAP	GENEINFO							
SEQUENCEVIEWER	ASSAYVIEWER	ASSAYVIEWER	GENE	FAM	MAP	GENEINFO	GENE	FAM	MAP	GENEINFO	GENE	FAM	MAP	GENEINFO							
ASSAYVIEWER	ASSAYVIEWER	ASSAYVIEWER	SPC	DOM	EXP	PUR	LOT	ASY	SPC	DOM	EXP	PUR	LOT	ASY	SPC	DOM	EXP	PUR	LOT	ASY	
EXP2255																					
Gene Info		UNQ753 PRO 1855 Human CTRP3 IgG TFDNA87982 FLDNA44686																			
EXP Lab Name		44686.221 JSF																			
DNA Lab Name		44686.221JSF Hif																			
Protein Request ID																					
System		Baculovirus																			
Virus Status																					
Exptd. Virus Harvest Date																					
Exptd. Harvest Date																					
Offmol																					
Fermentation Run ID																					
Cell Line		High5																			
Expression Media																					
Growth Factors																					
Supplements																					
Warning																					
Gels																					
Expressed		TRUE																			
Comments																					
Status																					
Date Entered		November 9, 1998																			
Date Canceled																					
Scientist		Bethanne Deuel																			
Notebook		0 -																			
Protein Lots																					
No LOTs for this EXPression																					

ASY | DNA | DOM | EXP | FAM | ELS | LIB | LOT | MAP | OLI | PRB | PRO | PUR | RNA | SRC | UNQ | XPI | YSI
 Assay Viewer | Sequence Viewer | Gene Viewer | GenenGenes | SAGE

GenenGenes Feedback

Appl. No. : 09/931,836
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EXHIBIT B—PAGE 4

GENENGENES		SITEMAP		Additional F	
GENE VIEWER	FAM MAP GENENOB	SEQUENCE VIEWER	SRC RNA LIB IRS UNQ	ASSAY VIEWER	SELECT EXP DOM PUR ASY
EXP2794					
Gene Info: UNQ753 PRO 4365 Human CTRP3 Poly-His TFDNA102368 FLDNA44686					
EXP Lab Name:	sst.44686.H8				
DNA Lab Name:	sst.44686.H8				
Protein Request ID:					
System:	Mammalian Stable				
Exptd. Harvest Date:					
Control:					
Fermentation Run ID:					
Cell Line:	CHO				
Expression Media:					
Growth Factors:					
Supplements:					
Warning:					
Gels:	<u>GEL180</u> <u>GEL181</u>				
Expressed:	FALSE				
Comments:	no band on western				
Status:					
Date Entered:	February 16, 1999				
Date Canceled:					
Scientist:	Ldney Lewis-Steiner				
Notebook:	30966 - 55				
Protein Lots:	No LOTS for this EXPression				

ASY | DNA | DOM | EXP | FAM | ELS | LIB | LOT | MAP | OLI | PRB | PRO | PUR | RNA | SRC | UNQ | XPT | YST
 Assay Viewer | Sequence Viewer | Gene Viewer | GenenGenes | SAGE

[GenenGenes Feedback](#)

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EXHIBIT C

(2 pages; pages 26-27)

Appl. No. : 09/931,836
Filed : August 16, 2001

EXHIBIT C—PAGE 1

GENEVIEWER		SEQUENCEVIEWER		PROTEINVIEWER		SEARCH	
GENE	PAM	MAP	GENEINFO	PROT	CDNA	ASY	SELECT
PROT	SPC	RNA	ASY	PDS	LOT		GO
CDNA	DON	EXP	PUR	LOT	ASY		SEARCH
PUR1009							
Gene Info		View Protein Record		View Process Record		Update Record	
Protein Request ID		UNQ753 PRO 1825 Human CTRP3 Poly-His TF DNA84665 FL DNA44686					
DNA Lab Name		pE44686-1		Protein Name			
PUR Name				Control			
Exped PUR Date		EXP		PUR Date		July 13, 1999	
Expd PUR Date		EXP2247		No Sequence Report Available			
Mass Spec		6.24 EU/ml		Sequence Info			
MW		1825.119		GEL S		GEL461	
Endotoxin Level		Approx. 31, 55 kDa		AA Analysis Std/ml			
HIS Molar Mass (kDa)		26723.56		OD 280			
Ext Coef (mM/L cm)				Endotoxin Units/OD 260 nm			
Protein ID				P10124-0000			
Reduced SDS MW							
Theoretical MW (kDa) RF#1							
Gel Score		1 mM HCl / 0.15 M NaCl / 4% mannitol					
Comments							
Status							
Date Entered		November 16, 1998		PUR Date			
Yield Concentration		4752 nM		Yield Volume		4.5ml	
Date Canceled				Cancel Reason			
Scientist		Corpuz, Racquel		Status		Done	
Delivered to				Origin			
Notes/Spec		32647-8-		Storage Location			
Protein Lot							

[ASY](#) | [DNA](#) | [DOM](#) | [EXP](#) | [FAM](#) | [FLS](#) | [LIB](#) | [LOT](#) | [MAP](#) | [OL](#) | [PRB](#) | [PRO](#) | [PUR](#) | [RNA](#) | [SRC](#) | [UNQ](#) | [XPT](#) | [YSI](#)
[Assay Viewer](#) | [Sequence Viewer](#) | [Gene Viewer](#) | [GenenGenes](#) | [SAGE](#)

GenenGenes Feedback

Appl. No. : 09/931,836
Filed : August 16, 2001

EXHIBIT C—PAGE 2

PUR1009

Gene Info UNQ753 PRO 1825 Human CTRP3 Poly-His [FDNA44686](#) [ELDNA44686](#)

Protein Request ID

DNA Lab Name pE44686-1

PUR Name:

Exptd. PUR Date

EXP [EXP2247](#)

No Sequence report available

Mass Spec

Warning

Endotoxin Level 6.24 EU/ml

LLS Molar Mass (g/mol)

Ext.Coeff. (mg/ml)¹(cm)⁻¹

Prot A ng/ml

Reduced SDS MW Approx. 31, 55 kDa

Theoretical MW of ORF#1 26723.56

Gel Score

Buffer 1 mM HCl / 0.15 M NaCl / 4% mannitol

Comments

Status

Date Entered November 16, 1998

Yield Concentration 4752 nM

Date Canceled

Scientist [Carmuz Recuel](#)

Delivered To

Notebook 32647-8

Storage Location

Protein Lots

[LOT2352](#) PIN1308-1 1009

ASY | DNA | DOM | EXP | FAM | FLS | LIB | LOT | MAP | OLI | PRB | PRO | PUR | RNA | SRC | UNQ | XPT | YSI
[Assay Viewer](#) | [Sequence Viewer](#) | [Gene Viewer](#) | [GenenGenes](#) | [SAGE](#)

[GenenGenes Feedback](#)

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EXHIBIT D

(3 pages; pages 29-31)

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EXHIBIT D—PAGE 1

UNQ753 PRO1825 Human CTRP3 Poly-His DNA84665 PUR1009 EXP2247

Some comment

August 5, 1999

1

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 Filed : August 16, 2001

EXHIBIT D—PAGE 2

<u>ASY64</u>	Retired	11/4/99	12/14/99	Proinflammatory/PMN Infiltrate
<u>ASY67</u>	Retired	9/2/99	9/28/99	MLR - Inhibitory
<u>ASY68</u>	On Hold	10/18/99	11/8/99	Hu Venous Endothelial Cell Ca Flux Assay
<u>ASY74</u>	Retired	9/28/99	11/8/99	Inhibition of Heart Neonatal Hypertrophy Induced by LIF+ET-1
<u>ASY75</u>	Retired	9/28/99	11/8/99	Enhancement of Heart Neonatal Hypertrophy Induced by LIF+4
<u>ASY100</u>	Running	8/20/99		Endotoxin Level (LAL)
<u>ASY103</u>	Running	9/1/99		Protein Gel Analysis
<u>ASY106</u>	Retired	10/2/99	12/1/99	Glucose and FFA uptake in Differentiated Skeletal Muscle
<u>ASY106</u>	Retired	12/3/99	1/4/00	Glucose and FFA uptake in Differentiated Skeletal Muscle
<u>ASY107</u>	Running	11/16/99	1/4/00	Fetal hemoglobin induction in an erythrobatic cell line
<u>ASY110</u>	Retired	10/22/99	11/10/99	Chondrocytes Re-differentiation Assay
<u>ASY110</u>	Retired	12/1/99	4/5/00	Chondrocytes Re-differentiation Assay
<u>ASY110</u>	Retired	12/15/99	3/27/00	Chondrocytes Re-differentiation Assay
<u>ASY110</u>	Retired	5/2/00	8/18/00	Chondrocytes Re-differentiation Assay
<u>ASY110</u>	Retired	5/16/00	8/18/00	Chondrocytes Re-differentiation Assay
<u>ASY111</u>	Retired	10/22/99	11/10/99	Chondrocyte Proliferation Assay
<u>ASY111</u>	Retired	12/1/99	4/5/00	Chondrocyte Proliferation Assay
<u>ASY111</u>	Retired	12/15/99	3/27/00	Chondrocyte Proliferation Assay
<u>ASY111</u>	Retired	5/2/00	8/18/00	Chondrocyte Proliferation Assay
<u>ASY111</u>	Retired	5/16/00	8/18/00	Chondrocyte Proliferation Assay
<u>ASY118</u>	Retired	1/12/00	2/1/00	Inhibition of A -Peptide Binding to Factor VIIa
<u>ASY119</u>	Retired	1/12/00	2/1/00	Inhibition of A - Peptide Binding to Factor VIIIE
<u>ASY128</u>	Retired	5/5/00	6/20/00	Cytokine Release in Human Whole Blood
<u>ASY129</u>	Retired	5/16/00	8/18/00	Chondrocytes re-differentiation by Fluorescence
<u>ASY130</u>	Retired	5/16/00	8/18/00	Chondrocytes Proliferation by fluorescence
<u>ASY132</u>	Retired	6/23/00	8/7/00	Activation of NFκB
<u>ASY134</u>	Retired	10/13/00	11/30/00	Activation of NFκB [Luciferase]
<u>ASY134</u>	Retired	12/5/00	1/22/01	Activation of NFκB [Luciferase]
<u>ASY135</u>	Retired	9/12/00	10/19/00	Induction of E-selectin
<u>ASY138</u>	Running	2/23/01	4/9/01	Normal Human Iliac Artery Endothelial cells

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EXHIBIT D—PAGE 3

ASY139	Running	2/23/01	4/9/01	Pooled Human Umbilical vein Endothelial cells
<u>ASY140</u>	Running	2/23/01	4/9/01	Coronary artery Smooth Muscle cells
<u>ASY141</u>	Running	2/23/01	4/9/01	Normal human Dermal Fibroblast Proliferation
<u>ASY142</u>	Running	2/14/01	3/26/01	NF-kappa B Inhibition Assay
<u>ASY142</u>	Running	3/8/01	3/26/01	NF-kappa B Inhibition Assay
<u>ASY146</u>	Running	7/19/01	8/3/01	Human Microvascular Endothelial Cell Proliferation Assay
<u>ASY162</u>	Running	11/16/09	9/5/00	NCI Oncology Screen-1
<u>ASY165</u>	Running	8/1/01	9/19/01	CREB
<u>ASY165</u>	Running	9/19/01	9/24/01	CREB
<u>ASY170</u>	Piloting	11/9/01	11/16/01	NHEK proliferation assay
<u>ASY174</u>	Piloting	3/12/02	4/3/02	Bovine Retinal M Endothelial
<u>ASY174</u>	Piloting	4/4/02		Bovine Retinal M Endothelial
<u>ASY174</u>	Piloting	5/17/02		Bovine Retinal M Endothelial
<u>ASY174</u>	Piloting	11/20/02		Bovine Retinal M Endothelial
<u>ASY175</u>	Running	12/21/01		Neuronal Differentiation using Rinat technology
<u>ASY175</u>	Running	5/30/02		Neuronal Differentiation using Rinat technology
<u>ASY176</u>	Piloting	5/31/02		Haemoglobin Assay
<u>ASY176</u>	Piloting	7/16/02		Haemoglobin Assay
<u>ASY177</u>	Piloting	4/22/03	8/18/03	fibroblast migration assay
<u>ASY178</u>	Running	1/23/03		Proliferation of Fibroblasts
<u>ASY180</u>	Running	3/11/03	3/25/03	Mouse Keratinocyte Assay
<u>ASY181</u>	Running	3/6/03	3/13/03	Human Mammary Epithelial Cell Assay
[REDACTED]				
ASY RNA Down EXP FAM FLS 4B LOT MAP Q1 PFB PRO PUR RNA SEC TINC XPT YST				
Assay Viewer Sequence Viewer Gene Viewer GenoGems SAGE				

GenoGems Feedback

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EXHIBIT E
(2 pages; pages 33-34)

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EXHIBIT E—PAGE 1

GENE/GENES		SEQUENCE		EXPERIMENT		Additional Resources:					
SEQUENCE VIEWER	GeneID: FA11 MAP: F1000000	SEQUENCE	AMINO ACIDS	SEQUENCE	AMINO ACIDS	SEQUENCE	AMINO ACIDS				
ASSAY VIEWER	AMINO ACIDS	AMINO ACIDS	AMINO ACIDS	AMINO ACIDS	AMINO ACIDS	AMINO ACIDS	AMINO ACIDS				
	FA11 - SRC	F1000000	LB1 - L15	OL1	PUR1 - PUR2	PUR1 - PUR2	PUR1 - PUR2				
	F1000000	AMINO ACIDS	EXPERIMENT	SEQUENCE	AMINO ACIDS	AMINO ACIDS	AMINO ACIDS				
	SELECT										
Assay Viewer											
<p>ASY1 Heart Neonatal Hypertrophy ASY2 Heart Adult Hypertrophy ASY3 Adipocyte Lipolysis ASY4 Adipocyte Lipogenesis ASY5 Hematopoiesis: stem cell proliferation ASY6 Hippocampal Neuron Survival ASY7 Retinal Neuron Survival (5-6 days cultur ASY8 Endothelial cell proliferation ASY9 Inhibition of VEGF stimulated endothelia ASY10 Eosinophil degranulation [induction of] ASY11 B cell IgE synthesis inhibition</p>											
<input type="checkbox"/> All Positives <input type="checkbox"/> Verified Positives <input type="checkbox"/> Pending				<input type="checkbox"/> To <input type="checkbox"/>							
ASSAY RESULT LIST											
ASY1	Chond Redfin	PUR1009	LOT252	PIN1308-1	47.50	nM	45.11	UNC0753	Human CTRP3 Poly-His	10/22/1999	11/10/1999
ASY1	Chond Redfin	PUR1009	LOT252	PIN1308-1	47.50	nM	72.58	UNC0753	Human CTRP3 Poly-His	12/5/1999	03/27/2000
ASY1	Chond Redfin	PUR1009	LOT252	PIN1308-1	47.50	nM	82.13	UNC0753	Human CTRP3 Poly-His	05/16/2000	06/16/2000
ASY1 DMSI DMSI EXP EAM EBS LB1 LOT1 MAP OL1 PUR1 PUR2 PUR3 BUR1 RNA1 SRC1 UNG1 LSI1 Assay Viewer Sequence Viewer Gene Viewer GridSearch SAGE											

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EXHIBIT E—PAGE 2